DENVER TB COURSE: CHALLENGING CLINICAL PRESENTATIONS

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OBJECTIVES

- Discuss complex cases
- Identify comorbid conditions that affect TB management
- Review how active TB might have been prevented
- Review how delays in diagnosis can be minimized

DISCLOSURES

- Has no significant financial interest to disclose

HPI

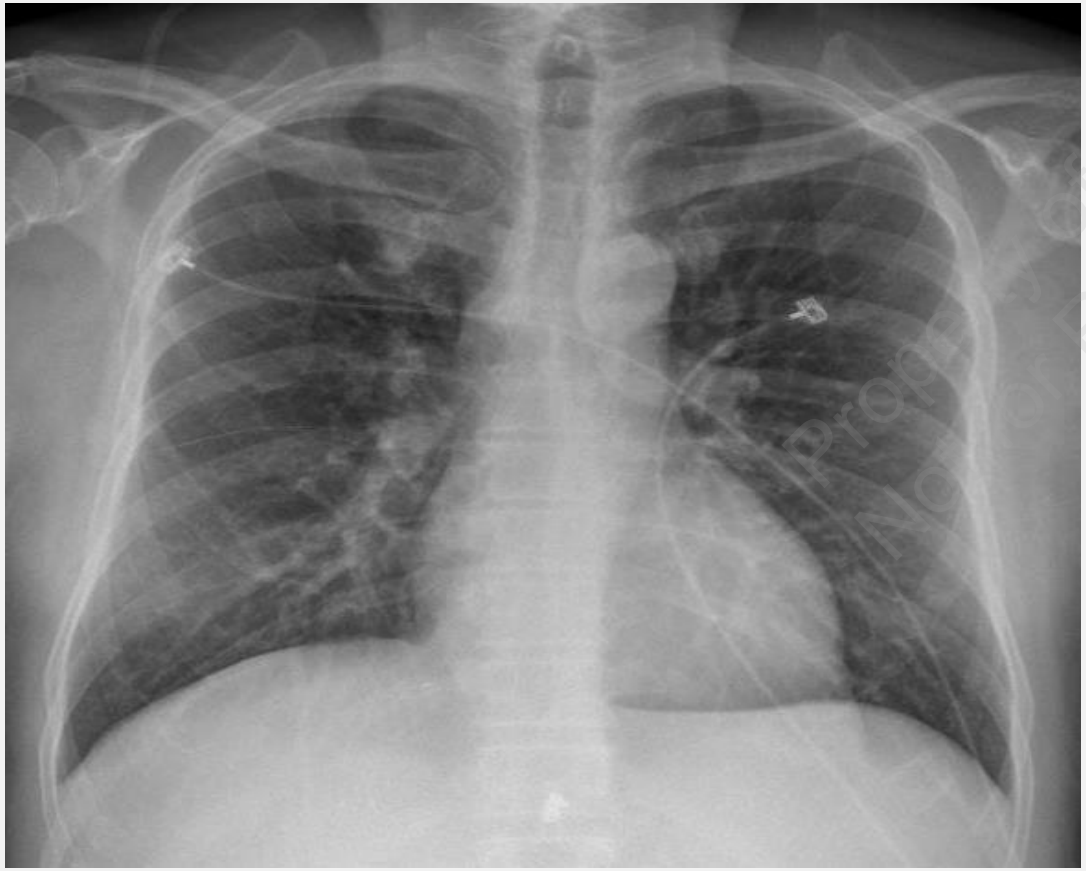
- 60 year old man with cryptogenic cirrhosis, associated TIPS placement is admitted with fevers, cough chronic right sided effusion and decompensated cirrhosis (MELD 24)
  - Started on vancomycin and cefepime for presumed HCAP
  - New murmur identified, TTE with possible mitral valve vegetation
  - Multiple blood cultures negative
  - ID consulted to assist with the evaluation of culture negative endocarditis

HPI

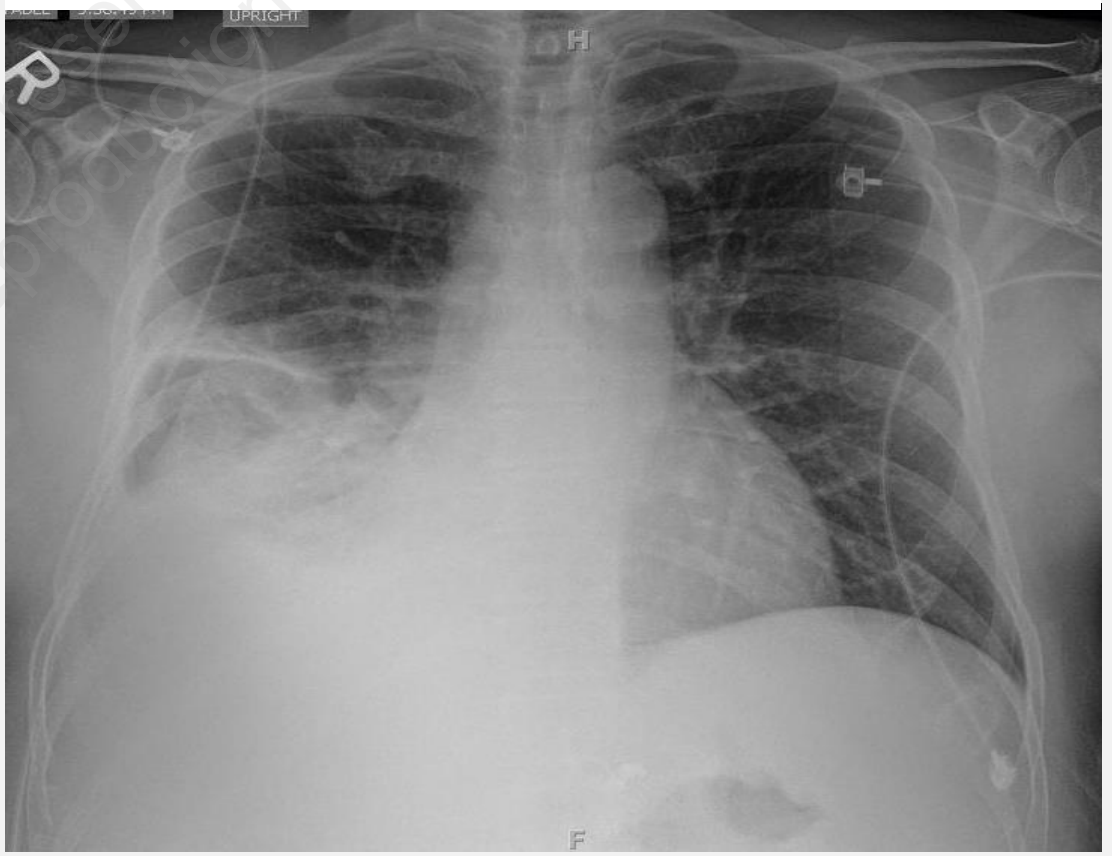
- ID spends the next few days pouring through his records
  - Originally from Mexico, living in the US for 18 years
  - Prior admission 2 months prior with sepsis and pneumonia. Found to have exudative pleural fluid, negative cultures
  - Remote history of presenting to TB clinic several years prior, IGRA testing done at that time was negative

HPI

6 MONTHS PRIOR DURING AN EPISODE OF GI BLEEDING



ADMISSION TWO MONTHS AGO WITH SEPSIS



HPI

Pleural fluid –

RBC 48,000

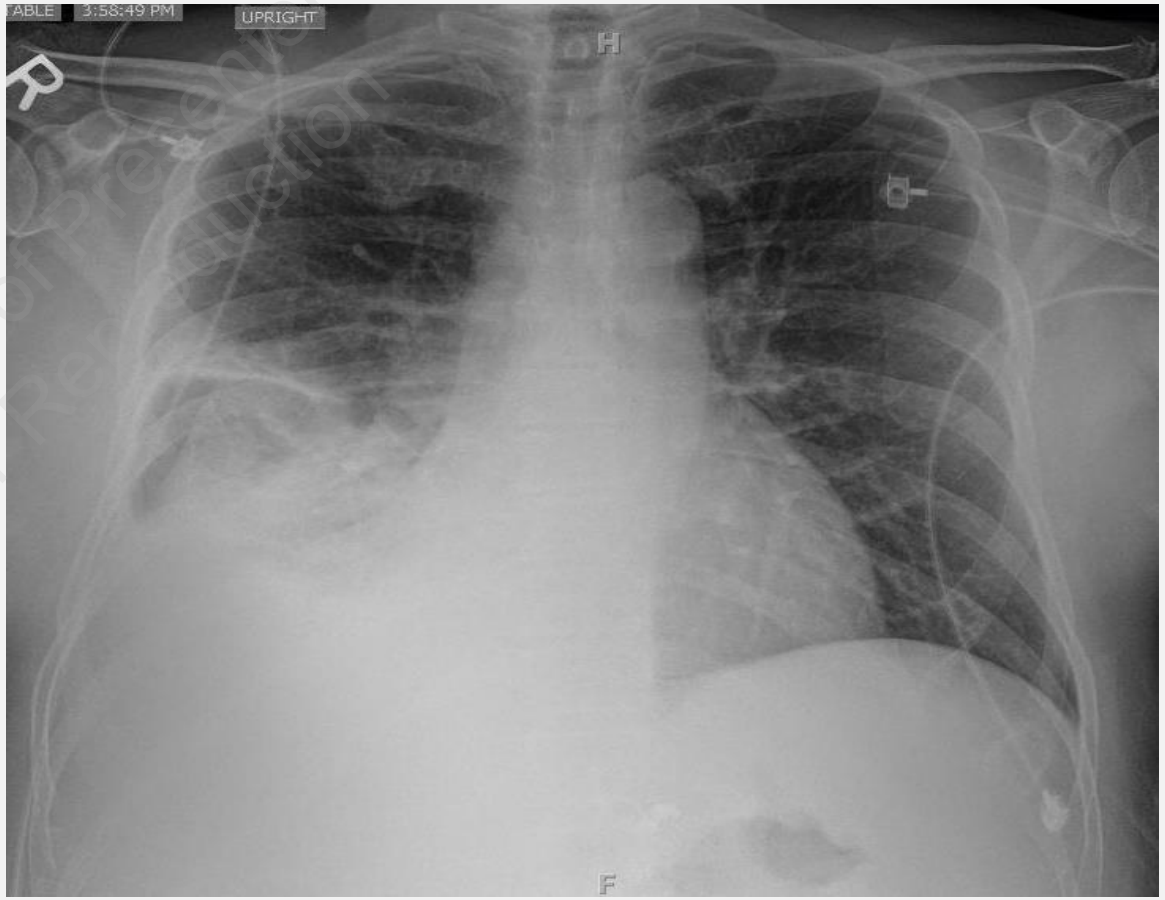
WBC 1,800 (73% L)

Prot 2.2

LDH 279 (serum 422)

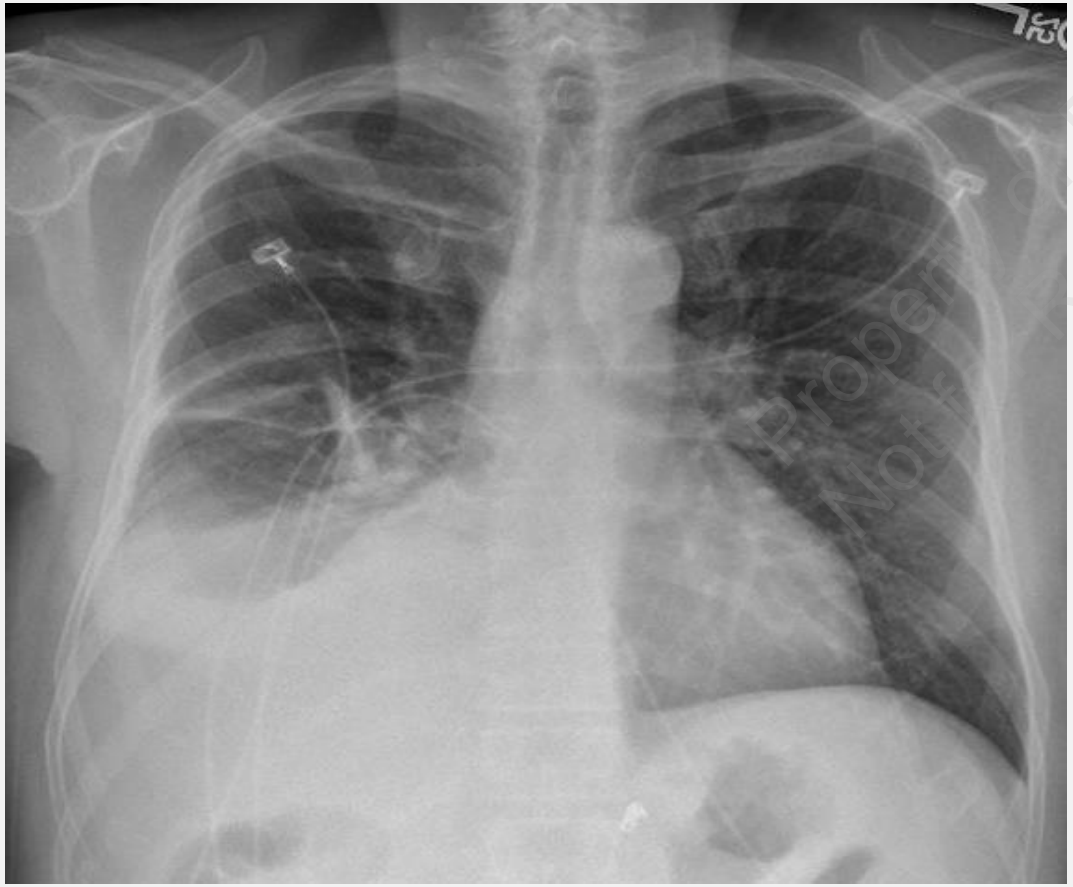
Procalcitonin < 0.05

Discharged on Levofloxacin, symptoms improve

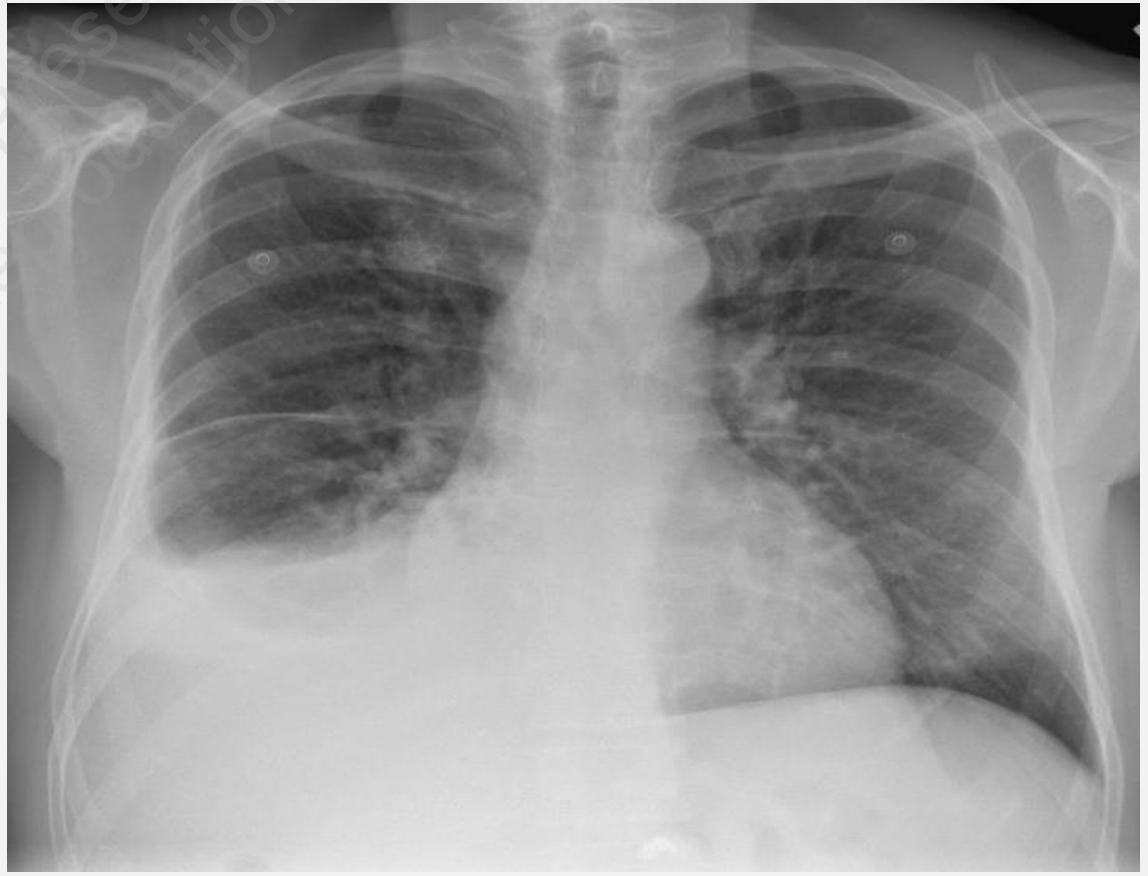


HPI

ONE MONTH AFTER SEPSIS EPISODE



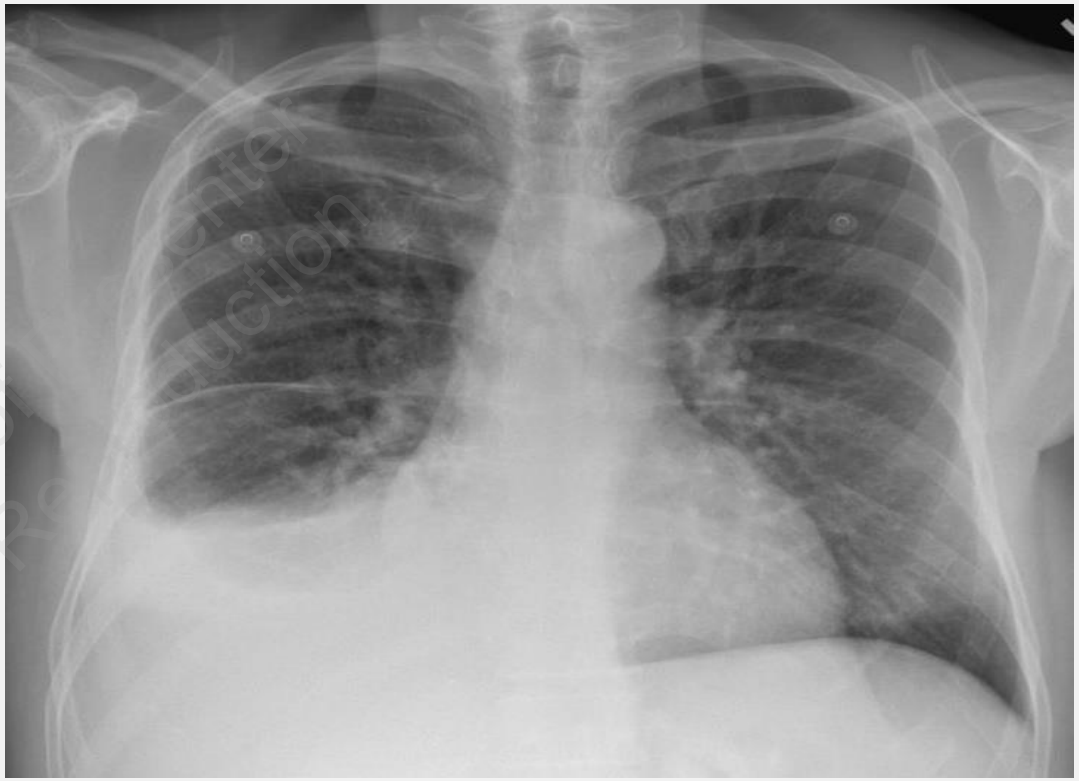
THIS ADMISSION



HPI

Pleural fluid – current admission

- pH 7.35
- Gluc 138
- RBC 46,000
- WBC 1,749 (78% L)
- Prot 2.5
- LDH 215 (serum 421)
- **ADA 2.1**



AFB cultures not sent on pleural fluid

HPI CONTINUED

- CBC
  - WBC 3.0
  - Hct 24.8
  - Platelets 68
- INR 2.5
- Cr 0.94

- LFTs
  - Total Bilirubin 5.0, direct 2.0
  - AST 50
  - ALT 28
  - Alb 1.2

Sputum 1+ AFB; Xpert (+) TB and Rifampin resistant

WHAT REGIMEN WOULD YOU RECOMMEND?

Any additional testing?

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HPI

- Treatment started with levofloxacin, amikacin, EMB, linezolid and imipenem
  - Imipenem discontinued after two weeks
  - QTc stable at 500
- MDDR-no INH resistance
- Phenotypic susceptibilities—rifampin and pyrazinamide resistance

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CLINICAL COURSE

treatment	regimen	notes
4 weeks	Levofloxacin, ethambutol, amikacin, linezolid	converts cultures at one month
	treatment held 2 weeks	developed perforated duodenum; AKI
6 weeks	Levofloxacin, ethambutol restarted followed by amikacin	Tolerates this well for some time; plan was to eventually stop amikacin
8-10 weeks	Levofloxacin, ethambutol, amikacin TIW, linezolid TIW	bili of 12, mostly indirect, HCT 24 to19, evidence of hemolysis. Platelets decrease to 18.
10 weeks	Levofloxacin, ethambutol, amikacin TIW	Linezolid felt to be contributing to anemia and thrombocytopenia
12 weeks	Levofloxacin, ethambutol, amikacin TIW	**need for other agents?**

WHAT WOULD YOU ADD AT THIS POINT?

A. Nothing, continue levofloxacin, ethambutol and amikacin
B. Clofazimine
C. Imipenem
D. Bedaquiline
E. Other not listed

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CLINICAL COURSE

treatment	regimen	notes
14 weeks	Levofloxacin, ethambutol, amikacin, **added clofazimine**	Stopped amikacin at 15 weeks
16-18 weeks	Levofloxacin, ethambutol, clofazimine	Develops right shoulder pain; reduced dose of levofloxacin to 500 mg; rotator cuff tear confirmed
18 -28 weeks	Levofloxacin, ethambutol, clofazimine	Worsening hepatohydrothorax, ascites and anasarca, estimated 40% mortality in 3 months (MELD 30); re-admitted

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CLINICAL COURSE AND OUTCOME

- Chooses hospice
- Died 30 weeks into treatment

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SUMMARY

- Treatment of drug-resistant TB in the context of cirrhosis is complex
  - Limited treatment options
  - Significant complications

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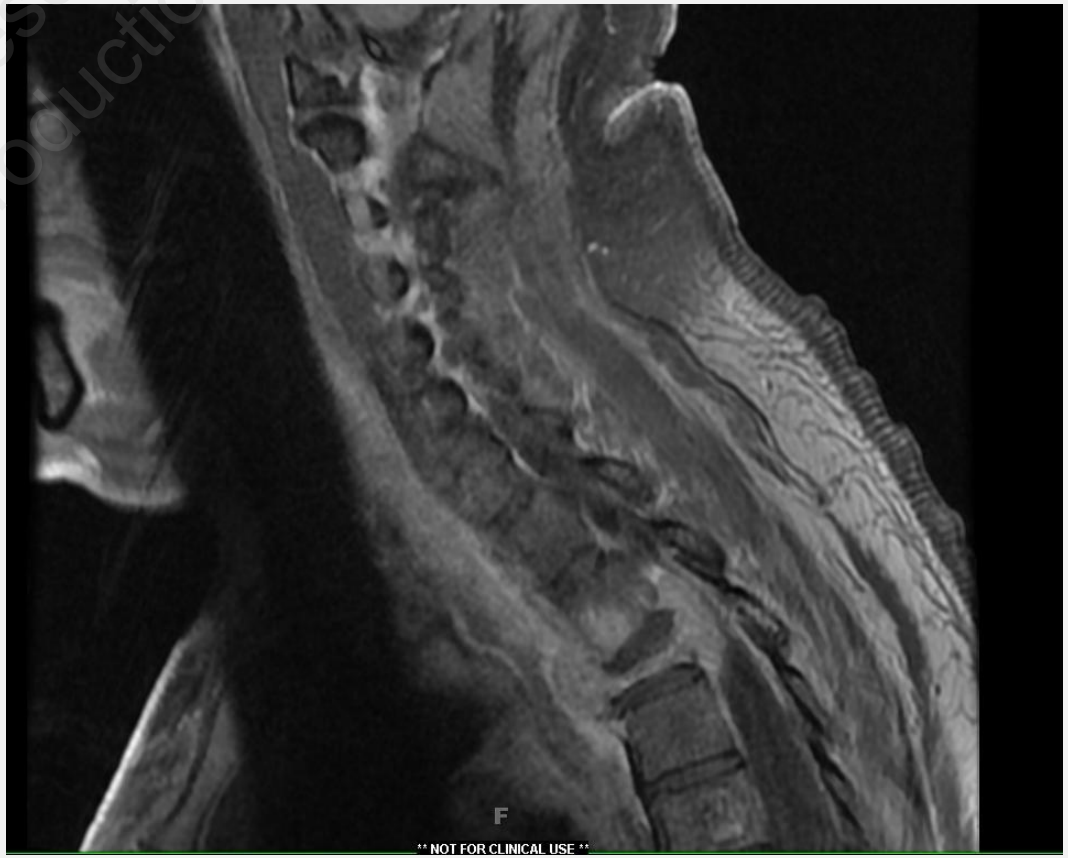
PATIENT # 2

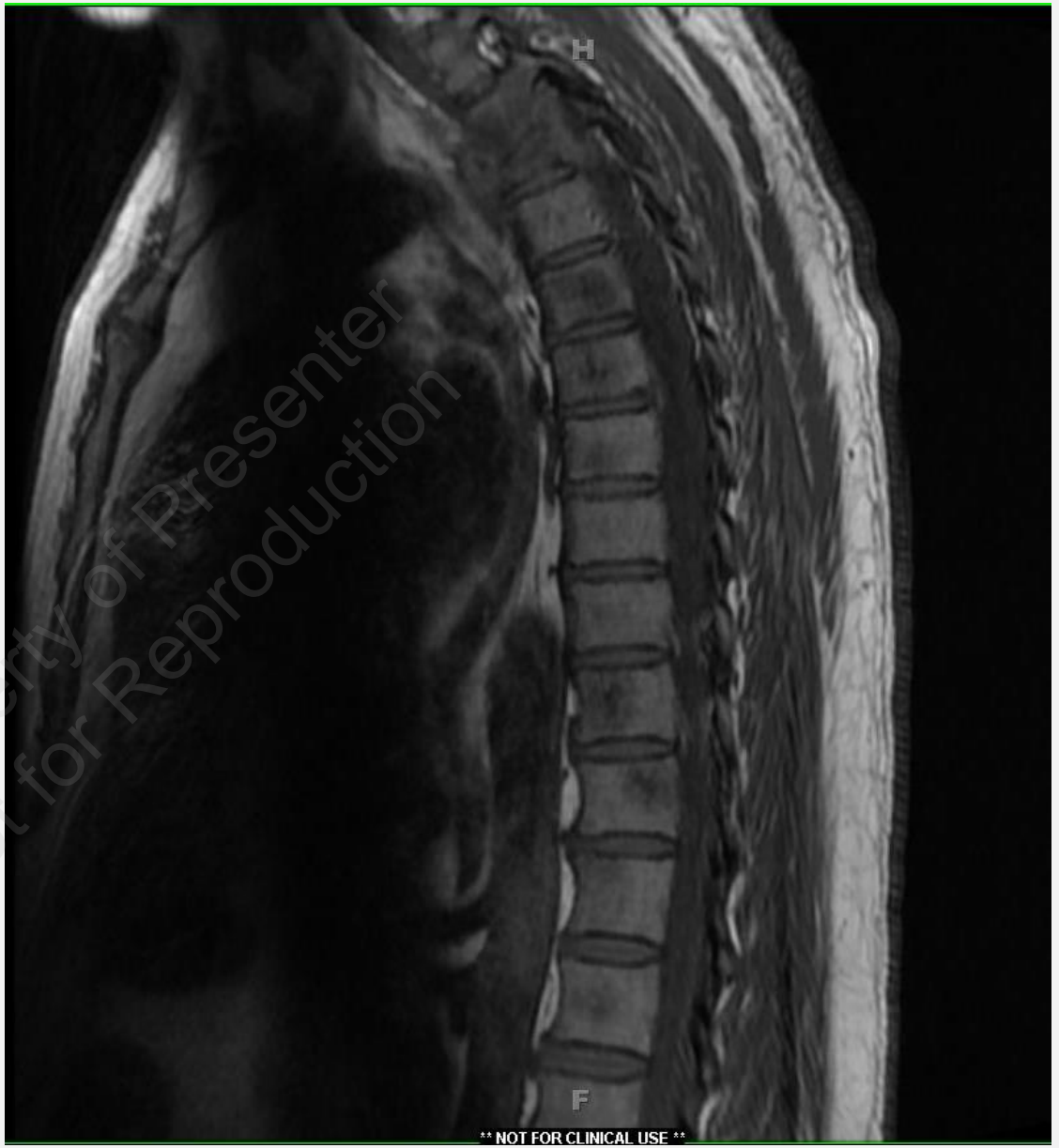
HPI

- 49 year old man with newly diagnosed type II diabetes who presented to an outside hospital with back pain and numbness/tingling in his legs bilaterally
  - No fever/chills
  - No weight loss
  - Vitals stable, afebrile
  - Exam without neurologic deficits

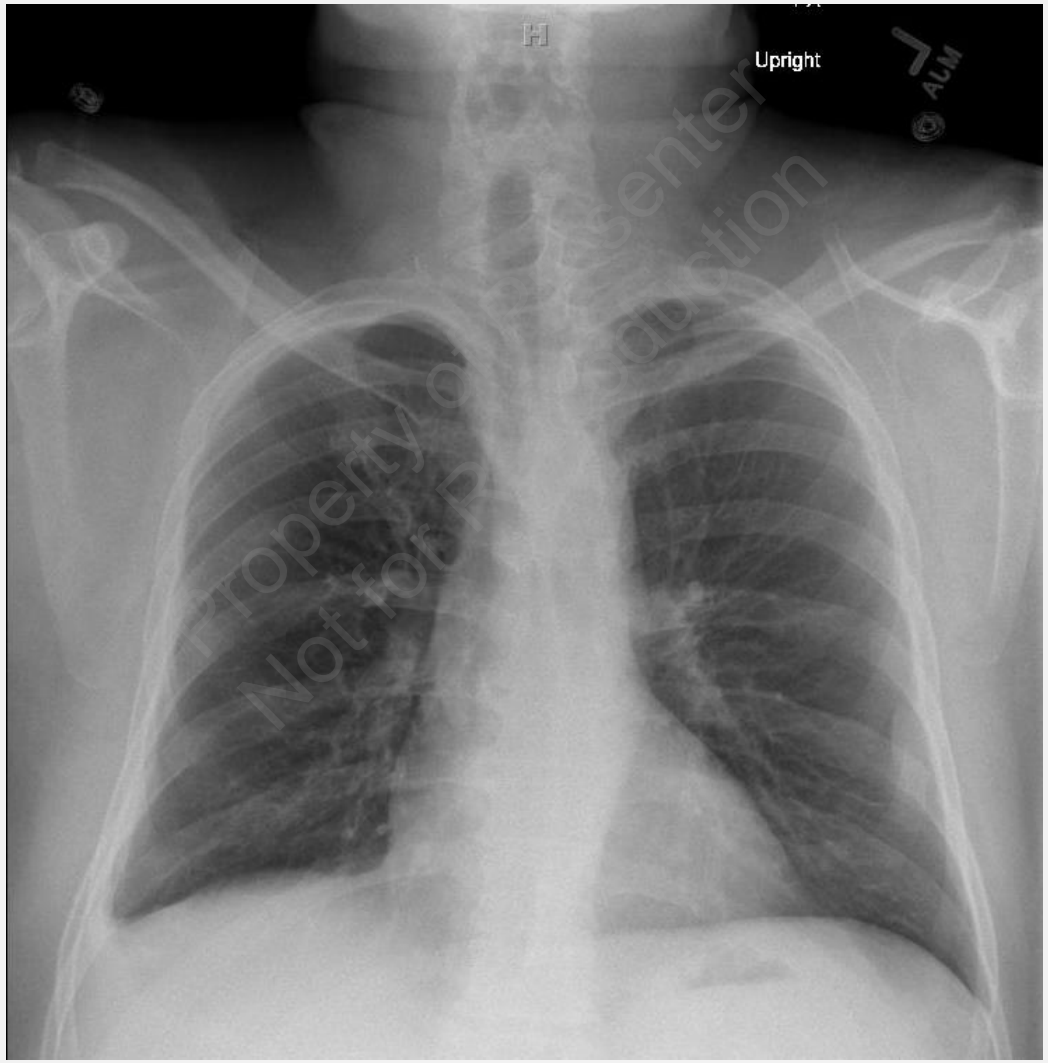


MRI report:

- “likely metastatic disease
- Pathologic 80% vertebral body fracture at T3, mass-like lesion with epidural extension of presumed tumor and retropulsion →severe canal stenosis



HPI

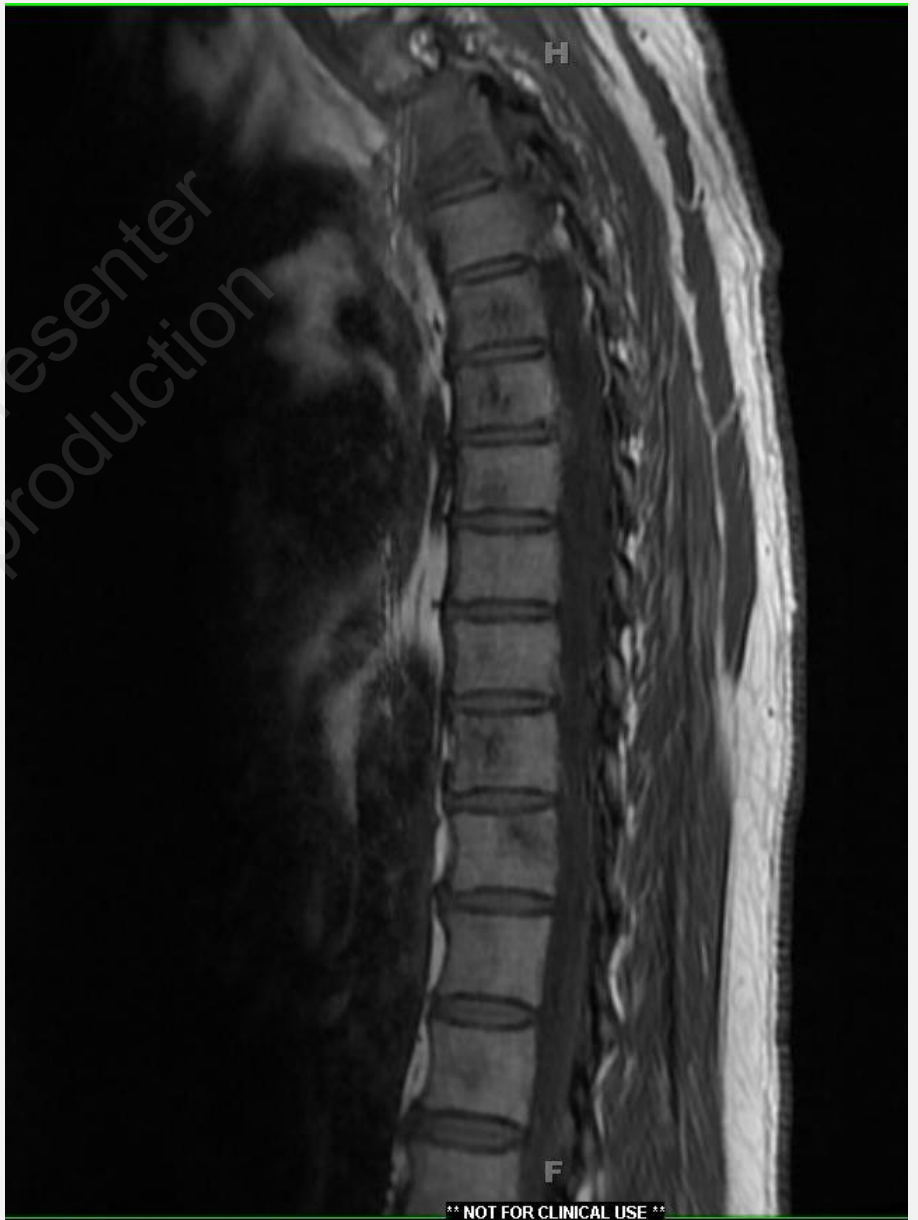


HPI

- Lived for years in Mexico, has been in the US since 2003
- No health insurance benefits through employment, doesn't qualify for health insurance under the ACA
- TST reportedly negative; HIV negative
- Underwent biopsy of T3:
  - Fibroadipose tissue and fragments of bone with prominent granulomatous inflammation
  - No evidence of malignancy, no AFB or fungal organisms
- Discharged home on the following:
  - Dexamethasone
  - Metformin

HPI

- Presents again 3 weeks later with:
  - Continued numbness and tingling of the entire bilateral LE's as well as unsteady gait
  - Worsening right sided upper back pain
  - IGRA positive
  - PSA 4.76 (>4 abnormal)



HPI

- Transferred to a referral center and admitted to neurosurgery
  - Underwent debulking with T3 corpectomy, T1-T5 spinal fusion, T2-4 decompression
- Concern for malignancy, PET scan ordered

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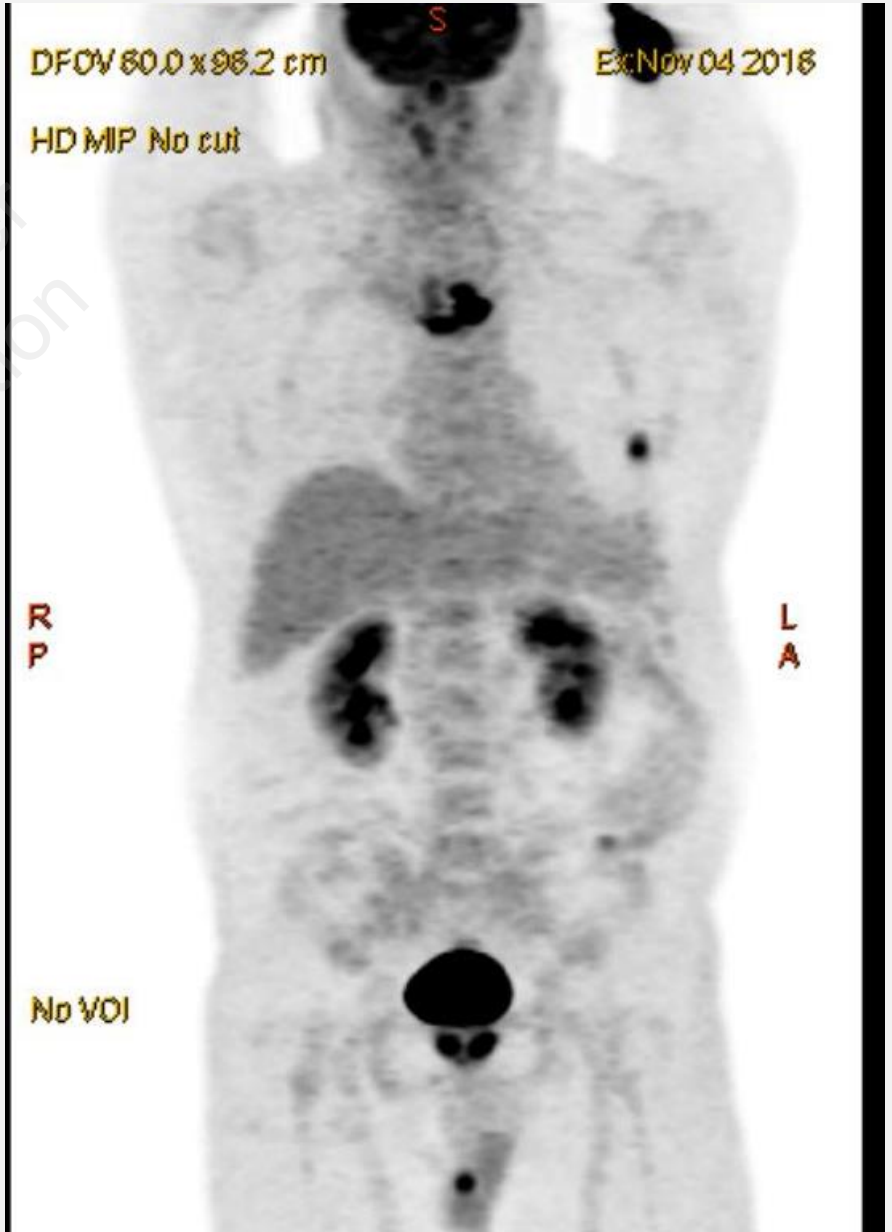
- Intense FDG activity in the following:
  - Soft tissues around the site of the T3 corpectomy
  - left lateral sixth rib lesion with likely pathologic fracture
  - Prostate
  - Right scrotum



DISCUSSION POINTS

- Are PET scan findings more consistent with metastatic cancer, TB or both?

- Is "granulomatous inflammation" enough to start active TB treatment in the context of a positive IGRA?

CLINICAL COURSE

- Excisional biopsy of left rib mass, and fluid sampling for culture
  - Blood and fibroadipose tissue.
- 2nd Rib biopsy:
  - Bone and bone marrow with extensive infiltration by non-caseating granulomas
    - No mycobacterial or fungal elements noted by AFB and GMS staining
- Prostate, right medial, right lateral, left medial and left lateral core biopsies:
  - Benign prostatic tissue with acute and chronic inflammation, foreign body giant cell reaction and abundant non-caseating granulomas

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- Patient was initiated on isoniazid, rifampin, pyrazinamide and ethambutol started
- PCR for *Mycobacterium tuberculosis (Mtb)* was positive from spinal mass/abscess fluid a few days later.
  - Culture positive, pan-susceptible
- Rib biopsy cultures negative for *Mtb*
- Urine culture negative for *Mtb*
- Sputum cultures negative *for Mtb*

COULD HIS ACTIVE TB BEEN PREVENTED?

- Meets criteria for TB preventative screening with IGRA:
  - From Mexico
  - Has uncontrolled diabetes
- Had been in the US for 14 years prior to developing active TB
- Possible barriers:
  - Lack of health insurance leading to challenges in receiving preventative care

SUMMARY

- Substantial overlap in the presentation of TB masquerading as metastatic disease
  - PET scan and MRI imaging was interpreted as consistent with metastatic disease
  - Biopsy of concerning lesions with findings clearly consistent with *Mtb* and not malignancy
- Delay in initiation of TB treatment related to substantial overlap in presentation with metastatic cancer
- Access to TB screening and treatment several years ago may have prevented him from developing active TB